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09/918,421	07/30/2001	Akira Suyama	01450/HG	6390

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 09/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/918,421

Applicant(s)

SUYAMA, AKIRA

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, filed 1 June 2005, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 6-12 are currently pending. Claims 1-5 have been cancelled.

Claim Objections

Claim 6 is objected to because of the following informalities: Claim 6 recites "the promising candidate nucleotide nucleotide sequences". "Nucleotide" is repeated twice. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

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Claim 6 is now directed to a method of selecting a promising candidate nucleotide sequence. However, there is no apparent support in the instant specification for a “promising candidate nucleotide” and none has been provided. The specification discloses “analytical sequences” (page 5, line 5) and “desired sequences” (page 2, line 4) but does not disclose a “promising candidate sequence”. The specification fails to disclose even the attributes of a sequence such that it could be a “promising” sequence. This limitation is new matter.

Furthermore, claim 6 now recites “the promising candidate nucleotide sequences have a high possibility of including a suitable nucleotide sequence of the analytical oligo nucleic acid”. The specification fails to describe such a limitation with regard to a “promising candidate”. This limitation introduces new matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of “undue experimentation”. These factors include: (a) the quantity of

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experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to select promising candidate nucleotide sequences using the steps of the instant claims. For the reasons discussed below, this constitutes undue experimentation.

b) and c) The specification provides a description of the instant invention in which the method is drawn to a method of determining a nucleotide sequence of an analytical oligonucleotide for analytical use. The steps include a first calculation step in which an occurrence frequency of each n unit sequence is determined. Secondly, an extraction step to form p sequences (p is larger than n , by at least 1). Third, a second calculation step is performed to determine an occurrence frequency within the p sequences, based upon the calculation of the n sequence frequency. Forth, a second extraction step is performed to gain a probe sequence that has a lower occurrence frequency than that obtained in the second calculation step (see pages 7 to 8). A group of low occurrence frequency candidate sequences extracted in the above steps is evaluated for conditions other than the occurrence frequency (that is, physicochemical conditions), thereby selecting a desired probe sequence. The probe sequence is not determined by the occurrence frequency alone.

The instant claims, however, do not reflect such steps. The instant claim steps are not enabled because one of skill in the art would not know how to use such steps to select a "promising" candidate. The first step in the instant claims is drawn to a first calculation of an

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occurrence frequency for n unit sequences, as above. The second step extracts all sequences, p, also as above. The third step calculates an occurrence frequency of candidate sequences, based upon the calculation in step (b) and the forth step selects from candidates those that have a lower occurrence frequency than a threshold.

In step (c) how are the candidates extracted? On what basis are they extracted? Is there a certain level of similarity to the target that needs to be obtained in order that the sequences are considered candidates? What are the criteria to be considered a candidate?

Furthermore, the instant claims are not enabling for the transition of step (e) to step (f), as it is not taught how to calculate an occurrence frequency index of a candidate on the basis of the occurrence of the n unit sequence. What parameters, criteria, or formulas are necessary to calculate the frequency index of the candidates based upon n units? On what is the threshold value based? Is it based upon a certain level of hybridization, for instance, as taught in the specification?

d) The invention is drawn to methods of selecting promising candidate nucleotides.

e) It would have been well known in the art that oligo probes can be designed based upon many criteria. For instance, Pazhitkov et al. (BMC Bioinformatics (2002) Vol. 3, pages 1-7) teach that species specific probes can be designed based upon a multiple alignment of sequences and that an algorithm may be employed to provide a function that calculates stability of matching oligos in dependence of the number and position of mismatches. The algorithm also provides a strategy for probe finding that scans all possible sequence combinations, and lastly the algorithm deals with matches caused by single nucleotide outloops of a given sequence (page 2, column 1). The algorithm is specific and includes equations for calculation of stability, as well as what the

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criteria for stability contain. Probes finding is detailed and sequential. The specific steps outlined enable one to design species-specific probes according to a specific design.

The instant **claims** lack enablement as the series of steps do not include the criteria necessary for one of skill in the art to use the invention.

f) The skill of those in the art of bioinformatics is high.

g) The prior art indicates that probe design requires detailed instruction in order to design stable probes.

h) The claims lack the teaching of how to get from steps (d) to (e), for instance, such that one of skill in the art could implement the invention. The skilled practitioner would first turn to the instant specification for guidance. However, the instant specification does not provide specific guidance to practice these embodiments as they are recited in the claims. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art teaches specific, well-defined steps for probe design that are not present in the instant claims. Finally, said practitioner would turn to trial and error experimentation. Such represents undue experimentation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 6 recites “promising candidate”. However, it is unclear as to the definition of “promising” in the claim. The specification is silent as to what defines a “promising” candidate. Is it the level of hybridization or some other criteria? Clarification is requested.

Claim 6 recites “suitable nucleotide”. It is unclear what defines “suitable”. The specification fails to teach what a suitable nucleotide entails. Is it a nucleotide sequence that is most likely to hybridize based upon evaluation criteria or some other definition? Furthermore, what is the oligo suitable for? Hybridization? Clarification is requested.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

No claims are allowed.

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Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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August 30, 2005
Lori A. Clow, Ph.D.
Art Unit 1631
Lori A. Clow

Marjorie A. Moran
8/31/05

MARJORIE A. MORAN
PRIMARY EXAMINER